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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,540	06/21/2001	Robert Klein	R-193/40338.119USU1	5814
23552	7590	10/06/2004	EXAMINER	
MERCHANT & GOULD PC P.O. BOX 2903 MINNEAPOLIS, MN 55402-0903			WILSON, MICHAEL C	
			ART UNIT	PAPER NUMBER

1632

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/887,540

Applicant(s)

KLEIN, ROBERT

Examiner

Michael C. Wilson

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 August 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 18 August 2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_

Claim(s) objected to: \_\_\_\_\_

Claim(s) rejected: 17-25Claim(s) withdrawn from consideration: 1-5 and 13-16

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
10. ☐ Other: \_\_\_\_\_

MICHAEL WILSON  
PRIMARY EXAMINER



***Response to Arguments***

**101**

Applicants argue knockout mice are used to determine the function of proteins. Applicants' argument is not persuasive. Knockout mice may not be capable of determine the function of the protein.

Bowery (Pharm. Rev., 2002, Vol. 54, pg 247-264) taught, "no unique pharmacological or functional properties have been assigned to either subunit or the variants" of GABA<sub>B</sub>. "The emergence of high-affinity antagonists for GABA<sub>B</sub> receptors has enabled a synaptic role to be established. However, than antagonists have generally failed to establish the existence of pharmacologically distinct receptor types within the GABA<sub>B</sub> receptor class. The advent of GABA<sub>B1</sub> knockout mice has also failed to provide support for multiple receptor types" (pg 247, col. 2, lines 4-). Therefore, knockout mice may not elucidate the role of the protein being knocked out.

Olsen (GABA in the Nervous System, 2000, pg 81-95) taught that "although gene targeting is often useful in delineating the contribution of a given gene product to phenotypic characteristics observed, some gene knockouts lead to embryonic or perinatal lethality, and others lead to no apparent phenotype. This can arise from a lack of any role for the gene in question in regard to the trait studies or from compensation by other gene products. Analysis of the compensation can yield valuable clues to the genetic pathway" (pg 82, last 11 lines of col. 1). Thus, knockout mice may only provide a clue to a pathway the protein being knocked out is involved in and not elucidate the function of the protein in the pathway – this is not a substantial utility. Knockout mice do

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not necessarily provide insight into the function of the protein. The phenotype of knockout mice does not necessarily reflect the role of the protein being knocked out because other proteins may compensate to cause the phenotype.

Applicants misinterpret the statement by the National Institute of Health.

"Researchers have utilized an array of innovative genetic technologies to [1] produce custom-made mouse models for a wide array of specific diseases, as well as [2] to study the function of targeted genes." NIH stated an array of genetic technologies was used to study the function of targeted genes; NIH did not state knockout mice were used to study the function of targeted genes. Mice with a disruption in a gene that correlated to a gene disruption in humans known to cause disease were clearly known in the art to be models of disease. In this case, using the mice to study gene function without describing the gene function has no utility. "Further research" to determine the function of the gene, how to use the mouse as a model of disease or how to identify compounds that alter a phenotype as described in the specification does not rise to the level of a substantial, credible or specific utility. Especially because wild-type mice can be used to study the function of a protein and to identify compounds that decrease anxiety, increase activity or decrease retinal degeneration as claimed.

Selling the mice claimed to three companies does not indicate the mice have utility in determining the function of the LRP5 gene because the mice may provide no useful data. The mice may not provide any information leading to the function of the LRP5 gene. Information gathered from the -/- LRP5 mice (e.g. identifying compounds that change the phenotype) may also be obtained from wild-type mice.

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The arguments provided under utility are new and excessive and could have been made during prosecution. After final consideration by the examiner is not intended to be exhaustively complete. For a thorough response to the numerous new arguments presented 8-18-04, a request for reconsideration should be filed.

***Claim Rejections - 35 USC § 112***

Applicants have not addressed the 112 enablement, written description and indefiniteness rejections.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.  
Michael C. Wilson



**MICHAEL WILSON  
PRIMARY EXAMINER**